

In the Claims

Please amend the claims as follows.

1. (Currently Amended) A synthetic nucleic acid molecule comprising at least 300 nucleotides of a coding region for a reporter polypeptide, wherein the codon composition of the synthetic nucleic acid molecule is different at more than 25% of the codons from that of a wild type nucleic acid sequence and encodes a reporter polypeptide which has at least 85% amino acid sequence identity to the reporter polypeptide encoded by the wild type nucleic acid ~~sequence molecule~~, wherein the codons which differ are selected so as to result in the synthetic nucleic acid molecule having a reduced number of a combination of transcription factor binding sequences, and intron splice sites, poly(A) addition sites and/or promoter sequences, relative to the wild type nucleic acid sequence, and wherein the synthetic nucleic acid molecule has reduced aberrant transcription relative to the transcription of the wild type nucleic acid sequence.
2. (Previously Presented) The synthetic nucleic acid molecule of claim 1 wherein the synthetic nucleic acid molecule has at least 5-fold fewer transcription factor binding sequences, intron splice sites, poly(A) addition sites and promoter sequences.
3. (Original) The synthetic nucleic acid molecule of claim 1 wherein the codon composition of the synthetic nucleic acid molecule differs from the wild type nucleic acid sequence at more than 35% of the codons.
4. (Original) The synthetic nucleic acid molecule of claim 1 wherein the codon composition of the synthetic nucleic acid molecule differs from the wild type nucleic acid sequence at more than 45% of the codons.

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5. (Original) The synthetic nucleic acid molecule of claim 1 wherein the codon composition of the synthetic nucleic acid molecule differs from the wild type nucleic acid sequence at more than 55% of the codons.
6. (Original) The synthetic nucleic acid molecule of claim 1 wherein the majority of codons which differ are ones that are preferred codons of a desired host cell.
- 7-8. (Cancelled)
9. (Original) The synthetic nucleic acid molecule of claim 1 wherein the synthetic nucleic acid molecule encodes a luciferase.
10. (Cancelled).
11. (Original) The synthetic nucleic acid molecule of claim 9 wherein the wild type nucleic acid sequence encodes a beetle luciferase.
12. (Original) The synthetic nucleic acid molecule of claim 11 wherein the synthetic nucleic acid molecule encodes the amino acid valine at position 224.
13. (Cancelled).
14. (Previously Presented) The synthetic nucleic acid molecule of claim 1 or 9 wherein the majority of codons which differ in the synthetic nucleic acid molecule are those which are employed more frequently in mammals.
15. (Previously Presented) The synthetic nucleic acid molecule of claim 1 or 9 wherein the majority of codons which differ in the synthetic nucleic acid molecule are those which are preferred codons in humans.

16-17. (Cancelled).

18. (Original) The synthetic nucleic acid molecule of claim 9 wherein the synthetic nucleic acid molecule comprises SEQ ID NO:7 (GRver5), SEQ ID NO:8 (GRver6), SEQ ID NO:9 (GRver5.1), or SEQ ID NO:297 (GRver5.1).

19. (Cancelled).

20. (Original) The synthetic nucleic acid molecule of claim 15 wherein the majority of codons which differ are the human codons CGC, CTG, TCT, AGC, ACC, CCA, CCT, GCC, GGC, GTG, ATC, ATT, AAG, AAC, CAG, CAC, GAG, GAC, TAC, TGC and TTC.

21. (Original) The synthetic nucleic acid molecule of claim 15 wherein the majority of codons which differ are the human codons CGC, CTG, TCT, ACC, CCA, GCC, GGC, GTC, and ATC or codons CGT, TTG, AGC, ACT, CCT, GCT, GGT, GTG and ATT.

22-23. (Cancelled).

24. (Original) The synthetic nucleic acid molecule of claim 1 wherein the synthetic nucleic acid molecule is expressed in a mammalian host cell at a level which is greater than that of the wild type nucleic acid sequence.

25. (Original) The synthetic nucleic acid molecule of claim 1 wherein the synthetic nucleic acid molecule has an increased number of CTG or TTG leucine-encoding codons.

26. (Original) The synthetic nucleic acid molecule of claim 1 wherein the synthetic nucleic acid molecule has an increased number of GTG or GTC valine-encoding codons.

27. (Original) The synthetic nucleic acid molecule of claim 1 wherein the synthetic nucleic acid molecule has an increased number of GGC or GGT glycine-encoding codons.

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28. (Original) The synthetic nucleic acid molecule of claim 1 wherein the synthetic nucleic acid molecule an increased number of ATC or ATT isoleucine-encoding codons.
29. (Original) The synthetic nucleic acid molecule of claim 1 wherein the synthetic nucleic acid molecule has an increased number of CCA or CCT proline-encoding codons.
30. (Original) The synthetic nucleic acid molecule of claim 1 wherein the synthetic nucleic acid molecule has an increased number of CGC or CGT arginine-encoding codons.
31. (Original) The synthetic nucleic acid molecule of claim 1 wherein the synthetic nucleic acid molecule has an increased number of AGC or TCT serine-encoding codons.
32. (Original) The synthetic nucleic acid molecule of claim 1 wherein the synthetic nucleic acid molecule has an increased number of ACC or ACT threonine-encoding codons.
33. (Original) The synthetic nucleic acid molecule of claim 1 wherein the synthetic nucleic acid molecule has an increased number of GCC or GCT alanine-encoding codons.
34. (Original) The synthetic nucleic acid molecule of claim 1 wherein the codons in the synthetic nucleic acid molecule which differ encode the same amino acids as the corresponding codons in the wild type nucleic acid sequence.
35. (Original) A plasmid comprising the synthetic nucleic acid molecule of claim 1.
36. (Original) An expression vector comprising the synthetic nucleic acid molecule of claim 1 linked to a promoter functional in a cell.
37. (Original) The expression vector of claim 36 wherein the synthetic nucleic acid molecule is operatively linked to a Kozak consensus sequence.

38. (Original) The expression vector of claim 36 wherein the promoter is functional in a mammalian cell.
39. (Original) The expression vector of claim 36 wherein the promoter is functional in a human cell.
40. (Cancelled).
41. (Original) The expression vector of claim 36 wherein the expression vector further comprises a multiple cloning site.
42. (Original) The expression vector of claim 41 wherein the expression vector comprises a multiple cloning site positioned between the promoter and the synthetic nucleic acid molecule.
43. (Original) The expression vector of claim 41 wherein the expression vector comprises a multiple cloning site positioned downstream from the synthetic nucleic acid molecule.
44. (Original) A host cell comprising the expression vector of claim 36.
45. (Previously Presented) A kit comprising, in suitable container means, the expression vector of claim 36, wherein the synthetic nucleic acid molecule encodes a reporter molecule.
46. (Cancelled).
47. (Previously Presented) A polynucleotide which hybridizes under medium stringency hybridization conditions to SEQ ID NO:22 (Rluc-final), SEQ ID NO:9 (GRver5.1), SEQ ID NO:18 (RD156-1H9), SEQ ID NO:297 (GRver5.1), SEQ ID NO:301 (RD156-1H9), or the complement thereof, and comprises an open reading frame encoding a luciferase polypeptide, wherein the codon composition of the open reading frame of the polynucleotide is different at

more than 25% of the codons from that of a wild type luciferase nucleic acid sequence and encodes a polypeptide which has at least 85% amino acid sequence identity to the polypeptide encoded by SEQ ID NO:22, SEQ ID NO:9, SEQ ID NO:18, SEQ ID NO:297, or SEQ ID NO:301, wherein the codons which differ are selected so as to result in the open reading frame in the polynucleotide having a reduced number of a combination of transcription factor binding sequences, and intron splice sites, poly(A) addition sites and/or promoter sequences relative to the wild type nucleic acid sequence.

48-59. (Cancelled).

60. (Original) The synthetic nucleic acid molecule of claim 1 wherein the synthetic nucleic acid molecule is expressed at a level which is at least 110% of that of the wild type nucleic acid sequence in a cell or cell extract under identical conditions.

61. (Previously Presented) The synthetic nucleic acid molecule of claim 1 wherein the reporter polypeptide encoded by the synthetic nucleic acid molecule has at least 90% contiguous sequence identity to the polypeptide encoded by the wild type nucleic acid sequence.

62. (Previously Presented) The synthetic nucleic acid molecule of claim 1 wherein the reporter polypeptide encoded by the synthetic nucleic acid molecule is identical in amino acid sequence to the polypeptide encoded by the wild type nucleic acid sequence.

63. (Previously Presented) A vector comprising a gene of interest and backbone sequences, wherein the backbone sequences comprise a synthetic nucleic acid molecule having at least 3-fold fewer regulatory sequences relative to a parent nucleic acid sequence, wherein the sequences which are fewer are a combination of transcription factor binding sequences, and intron splice sites, poly(A) addition sites and/or promoter sequences, and wherein the synthetic nucleic acid molecule has reduced aberrant transcription relative to the transcription of the parent nucleic acid sequence.

64. (Original) The vector of claim 63 wherein the synthetic nucleic acid molecule does not encode a polypeptide.

65-66. (Cancelled).

67. (Currently Amended) A synthetic nucleic acid molecule comprising at least 300 nucleotides of a coding region for a luciferase, wherein the codon composition of the synthetic nucleic acid molecule is different at more than 25% of the codons from that of a wild type nucleic acid sequence and encodes a luciferase which has at least 85% amino acid sequence identity to the luciferase encoded by the wild type nucleic acid sequence ~~molecule~~, wherein the codons which differ are selected so as to result in a synthetic nucleic acid molecule having a reduced number of a combination of mammalian transcription factor binding sequences, and intron splice sites, poly(A) addition sites and/or promoter sequences relative to the wild type nucleic acid sequence, wherein the synthetic nucleic acid molecule has reduced aberrant transcription relative to the transcription of the wild type nucleic acid sequence, and wherein the codons which differ are codons which are employed more frequently in mammals.

68. (Previously Presented) The synthetic nucleic acid molecule of claim 1 or 67 which has at least 3-fold fewer sequences, wherein the sequences which are fewer are a combination of transcription factor binding sequences, and intron splice sites, poly(A) addition sites, and/or promoter sequences.

69. (Previously Presented) The synthetic nucleic acid molecule of claim 11 or 67 which has 74% or less nucleic acid sequence identity to the wild type nucleic acid sequence.

70. (Previously Presented) The synthetic nucleic acid molecule of claim 11 or 67 which has at least 40-fold increased expression relative to the wild type nucleic acid sequence.

71. (Previously Presented) The polynucleotide of claim 47 which hybridizes under high stringency hybridization conditions to SEQ ID NO:22 (Rluc-final), SEQ ID NO:9 (GRver5.1),

SEQ ID NO:18 (RD156-1H9), SEQ ID NO:297(GRver5.1), SEQ ID NO:301 (RD156-1H9), or the complement thereof.

72. (Previously Presented) The synthetic nucleic acid molecule of claim 11 or 67 wherein the codons are selected to reduce the introduction of transcription factor binding sequences, poly(A) addition sites, intron splice sites or promoter sequences.

73. (Previously Presented) A synthetic nucleic acid molecule comprising at least 300 nucleotides of a coding region for a reporter polypeptide and at least a portion of a vector backbone, wherein the nucleic acid sequence of the synthetic nucleic acid molecule is different than the nucleic acid sequence of a nucleic acid molecule which encodes a wild type reporter polypeptide and at least a portion of a vector backbone, wherein the codon composition of the coding region in the synthetic nucleic acid molecule is different at more than 25% of the codons from that of a coding region for the wild type reporter polypeptide and encodes a reporter polypeptide which has at least 85% amino acid sequence identity to the wild type reporter polypeptide, wherein the nucleic acid sequence in the synthetic nucleic acid molecule is selected so as to result in the synthetic nucleic acid molecule having a reduced number of a combination of transcription factor binding sequences, and intron splice sites, poly(A) addition sites and/or promoter sequences, relative to the nucleic acid molecule which encodes a wild type reporter polypeptide and at least a portion of a vector backbone, and wherein the synthetic nucleic acid molecule has reduced aberrant transcription relative to the transcription of the nucleic acid molecule which encodes a wild type reporter polypeptide and at least a portion of a vector backbone.

74. (New) A synthetic nucleic acid molecule comprising at least 300 nucleotides of a coding region for a luciferase, wherein the codon composition of the synthetic nucleic acid molecule is different at more than 25% of the codons from that of a parent nucleic acid sequence and encodes a luciferase which has at least 85% amino acid sequence identity to the luciferase encoded by the parent nucleic acid sequence, wherein the codons which differ are selected so as to result in a synthetic nucleic acid molecule which has reduced aberrant transcription relative to

the transcription of the parent nucleic acid sequence, and wherein the codons which differ are codons which are employed more frequently in mammals.

75. (New) The synthetic nucleic acid molecule of claim 74 wherein the parent nucleic acid sequence is SEQ ID NO:2.

76. (New) The synthetic nucleic acid molecule of claim 74 wherein the polypeptide encoded by the synthetic nucleic acid molecule has at least 95% amino acid identity to the luciferase encoded by the parent nucleic acid sequence.

77. (New) The synthetic nucleic acid molecule of claim 74 which has 74% or less nucleic acid sequence identity to the parent nucleic acid sequence.

78. (New) A polynucleotide which hybridizes under medium stringency hybridization conditions to SEQ ID NO:9 (GRver5.1) or SEQ ID NO:297 (GRver5.1), or the complement thereof, and comprises an open reading frame encoding a luciferase polypeptide, wherein the codon composition of the open reading frame of the polynucleotide is different at more than 25% of the codons from that of a parent luciferase nucleic acid sequence and encodes a polypeptide which has at least 85% amino acid sequence identity to the polypeptide encoded by SEQ ID NO:9 or SEQ ID NO:297, wherein the codons which differ are selected so as to result in a polynucleotide which has reduced aberrant transcription relative to the transcription of the parent nucleic acid sequence, and wherein the codons which differ are codons which are employed more frequently in mammals.

79. (New) The polynucleotide of claim 78 wherein the parent nucleic acid sequence has SEQ ID NO:2.

80. (New) The polynucleotide of claim 78 wherein the polypeptide encoded by the polynucleotide has at least 95% amino acid identity to the luciferase encoded by the parent nucleic acid molecule.